In the Claims:

1. (Original) A method for diagnosing a pre-clinical status, or a clinical status of a mucopolysaccharidoses ("MPS") disease in a target animal comprising:

(a) determining a target quantity of a target MPS biomarker from a target biological sample taken from the target animal; and

(b) comparing the target quantity to a reference quantity of a reference MPS biomarker;

wherein,

the target MPS biomarker is the same or equivalent to the reference MPS biomarker, and each of the target MPS biomarker and the reference MPS biomarker is an oligosaccharide;

the reference quantity is determined from a reference animal, or group of reference animals, having a known MPS clinical status;

the target quantity and the reference quantity are determined by a mass spectrometric analysis; and

a deviation of the target quantity of the target MPS biomarker from the reference quantity of the reference MPS biomarker is a pre-clinical or clinical indication of the MPS disease, an indication of a progression of the MPS disease, or an indication of a regression of the MPS disease.

2. (Original) The method of claim 1, wherein the target biological sample or reference biological sample is selected from a cellular extract, blood, plasma, or urine.

3. (Original) The method of claim 1, further comprising derivatizing the target MPS biomarker and the reference MPS biomarker with a derivatizing agent prior to determining the quantity of the target MPS biomarker or the quantity of the reference MPS biomarker.

4. (Ori ginal) The method of claim 3, wherein the derivatizing agent comprises 1- phenyl-3-methyl-5-pyrazolone ("PMP").

5. (Ori ginal) The method of claim 1, wherein the oligosaccharide comprises a sulfated saccharide molecule having a sugar length ranging from 1 to 12 residues.

6. (Ori ginal) The method of claim 1, wherein the oligosaccharide identified from the target biological sample comprises a cleavage product of a glycosaminoglycan ("GAG").

7. (Ori ginal) The method of claim 6, wherein the GAG is heparan sulfate, dermatan sulfate, keratan sulfate, or chondroitin sulfate.

8. (Ori ginal) The method of claim 1, wherein the oligosaccharide is a dermatan sulfate fragment that comprises: IdoA-(GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-11; IdoA-(GalNAc-UA)$_n$(S)$_m$, wherein, n=1-6, m-0-12; IdoA2S-(GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-11; IdoA2S-(GalNAc-UA)$_n$(S)$_m$, wherein, n=1-6, m=0-12; GalNAc4S-(UA-(GalNAc-UA)$_n$)(S)$_m$, wherein, n=0-5, m=0-12; GalNAc4S-(UA-GalNAc)$_n$(S)$_m$,

wherein, n=0-6, m=0-13; GlcA-GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-11; or GlcA-(GalNAc-UA)$_n$(S)$_m$,

wherein, n=0-6, m=0-12; wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine, GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

9. (Ori ginal) The method of claim 1, wherein the oligosaccharide is a heparan sulfate fragment that comprises: IdoA-(GlcNAc/GlcN-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; IdoA-(GlcNAc/GlcN-UA)$_n$(S)$_m$, n=1-6, m=0-18; IdoA2S-(GlcNAc/GlcN-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; IdoA2S-(GlcNAc/GlcN-UA)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNS-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNS-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNAc-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNAc-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcN-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcN-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNAc6S/GlcN6S-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNAc6S/GlcN6S-(UA-(GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-6, m=0-18; GlcA-(GlcNAcS/GlcNS-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; or GlcA-(GlcNAc/GlcN-UA)$_n$(S)$_m$, wherein n=0-6, m=0-18;

wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

10. (Original) The method of claim 1, wherein the oligosaccharide is a keratan sulfate fragment that comprises: Gal6S-(GlcNAc-(Gal-GlcNAc)$_n$)(S)$_m$, wherein n=0-5, m=0-11; Gal6S-(GlcNAc-Gal)$_n$(S)$_m$, wherein n=0-6, m=0-12; Gal-(GlcNAc-(Gal-GlcNAc)$_n$)(S)$_m$, wherein n=0-5, m=0-11; or Gal-(GlcNAc-Gal)$_n$(S)$_m$, wherein n=1-6, m=0-12;

wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

11. (Original) The method of claim 1, wherein the oligosaccharide is a chondroitin sulfate fragment selected from GalNAc6S-(UA-(GalNAc-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-11; or GalNAc6S-(UA-GalNAc)$_n$(S)$_m$, wherein n=0-6, m=0-12;

wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

12. (Original) The method of claim 1, wherein the mass spectrometry comprises electrospray-ionization tandem mass spectrometry ("ESI-MSMS") or liquid chromatography tandem mass spectrometry ("LC-MSMS").

13. (Original) The method of claim 1, wherein the mass spectrometry is carried out in conjunction with an immunoassay, liquid chromatography, anion exchange chromatography, or combination thereof.

14. (Original) The method of claim 1, wherein the target quantity and the reference quantity are normalized to creatinine or another oligosaccharide.

15. (Original) The method of claim 1, wherein the target animal has received an MPS therapy.

16. (Original) The method of claim 15, wherein the MPS therapy comprises a bone marrow transplant ("BMT") or a MPS enzyme replacement therapy.

17. (Original) The method of claim 1, further comprising treating the target animal with a MPS therapy, wherein the MPS therapy is based on the deviation of the target quantity as compared to the reference quantity.

18. (Original) The method of claim 17, wherein the MPS therapy comprises a bone marrow transplant ("BMT") or a MPS enzyme replacement therapy.

19. (Original) The method of claim 1, wherein the target biological sample and the reference biological sample contain an internal standard

20. (Original) The method of claim 19, wherein the internal standard comprises a deuterated N-acetylglucosamine-6-sulfate ("GlcNAc6S(d3)").

21. (Original) The method of claim 19, wherein the internal standard comprises a non-physiological oligosaccharide that is similar to the oligosaccharide being investigated.

22. (Original) The method of claim 21, wherein the non-physiological oligosaccharide is derived from a chondroitinase digestion of chondroitin sulfate having an unsaturated uronic acid at the non-reducing end.

23. (Original) The method of claim 1, wherein the MPS disease is MPS-I, MPS-II, MPS-IIIA, MPS-IIIB, MPS-VI, MPS-IIIC, MPS-IIID, MPS-IV, or combination thereof.

24. (Original) The method of claim 1, wherein the target animal is a newborn baby.

25. (Original) The method of claim 1, wherein the target MPS biomarker is contacted with a an enzyme that characterizes a particular MPS disease subtype, wherein contacting occurs before determining the target quantity.

26. (Original) The method of claim 25, wherein the enzyme comprises α-L-iduronidase.

27. (Original) A method for diagnosing a preclinical status, or a clinical status, of a mucopolysaccharidoses ("MPS") disease in a target animal comprising:

(a) derivatizing a target MPS biomarker with a derivatizing agent forming a derivatized target MPS biomarker;

(b) binding the derivatized target MPS biomarker to an extraction compound to give a bound derivatized target MPS biomarker;

(c) eluting the bound derivatized target MPS biomarker from the extraction compound with an elution solution forming an eluted target MPS biomarker;

(d) determining a target quantity of the eluted target MPS biomarker; and

(e) comparing the target quantity with a reference quantity of a reference MPS biomarker;

wherein,

the target MPS biomarker was obtained from a biological sample of a target animal having the MPS biomarker contained therein;

the target MPS biomarker is the same or equivalent to the reference MPS biomarker, and each of the target MPS biomarker and the reference MPS biomarker is an oligosaccharide;

the reference quantity is determined in a reference animal, or group of reference animals having a known MPS clinical status; and

a deviation in the quantity of the eluted target MPS biomarker when compared to the reference quantity is a pre-clinical or clinical indication of the MPS disease, a progression of the MPS disease, or a regression of the MPS disease.

28. (Original) The method of claim 27, wherein the target biological sample or reference biological sample is selected from a cellular extract, blood, plasma, or urine.

29. (Original) The method of claim 27, further comprising lyophilizing the target biological sample prior to derivatizing the target MPS biomarker.

30. (Original) The method of claim 27, wherein the derivatizing agent comprises 1-phenyl-3-methyl-5-pyrazolone ("PMP").

31. (Original) The method of claim 27, wherein the oligosaccharide comprises a sulfated saccharide molecule having a sugar length ranging from 1 to 12 residues.

32. (Original) The method of claim 27, wherein the oligosaccharide identified from the target biological sample comprises a cleavage product of a glycosaminoglycan ("GAG").

33. (Original) The method of claim 32, wherein the GAG is heparan sulfate, dermatan sulfate, keratan sulfate, or chondroitin sulfate.

34. (Original) The method of claim 27, wherein the oligosaccharide is a dermatan sulfate fragment that comprises: IdoA-(GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-11; IdoA-(GalNAc-UA)$_n$(S)$_m$, wherein, n=1-6, m=0-12; IdoA2S-(GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-11; IdoA2S-(GalNAc-UA)$_n$(S)$_m$, wherein, n=1-6, m=0-12; GalNAc4S-(UA-(GalNAc-UA)$_n$)(S)$_m$, wherein, n=0-5, m=0-12; GalNAc4S-(UA-GalNAc)$_n$(S)$_m$, wherein, n=0-6, m=0-13; GlcA-GalNAc-(UA-GalNAc)$_n$)(S)$_m$, wherein, n=0-5, m=0-1; or GlcA-(GalNAc-UA)$_n$(S)$_m$, wherein, n=0-6, m=0-12;

wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

35. (Original) The method of claim 27, wherein the oligosaccharide is a heparan sulfate fragment that comprises: IdoA-(GlcNAc/GlcN-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; IdoA-(GlcNAc/GlcN-UA)$_n$(S)$_m$, n=1-6, m=0-18; IdoA2S-(GlcNAc/GlcN-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; IdoA2S-(GlcNAc/GlcN-UA)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNS-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNS-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNAc-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNAc-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcN-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcN-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=1-6, m=0-18; GlcNAc6S/GlcN6S-(UA-(GlcNAc/GlcN-UA)$_n$)(S)$_m$, wherein n=0-5, m=0-16; GlcNAc6S/GlcN6S-(UA-GlcNAc/GlcN)$_n$(S)$_m$, wherein n=0-6, m=0-18; GlcA-(GlcNAcS/GlcNS-(UA-GlcNAc/GlcN)$_n$)(S)$_m$, wherein n=0-5, m=0-17; or GlcA-(GlcNAc/GlcN-UA)$_n$(S)$_m$, wherein n=0-6, m=0-18;

wherein, IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

36. (Original) The method of claim 27, wherein the oligosaccharide is a keratan sulfate fragment that comprises: Gal6S-(GlcNAc-(Gal-GlcNAc)$_n$)(S)$_m$, wherein n=0-5, m=0-11; Gal6S-

$(GlcNAc\text{-}Gal)_n(S)_m$, wherein n=0-6, m=0-12; $Gal\text{-}(GlcNAc\text{-}(Gal\text{-}GlcNAc)_n)(S)_m$, wherein n=0-5, m=0-11; or $Gal\text{-}(GlcNAc\text{-}Gal)_n(S)_m$, wherein n=1-6, m=0-12;

wherein,

IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

37. (Original) The method of claim 27, wherein the oligosaccharide is a chondroitin sulfate fragment selected from $GalNAc6S\text{-}(UA\text{-}(GalNAc\text{-}UA)_n)(S)_m$, wherein n=0-5, m=0-11; or $GalNAc6S\text{-}(UA\text{-}GalNAc)_n(S)_m$, wherein n=0-6, m=0-12;

wherein,

IdoA=iduronic acid; GlcA=glucuronic acid; GalNAc=N-acetylgalactosamine; GlcNAc=N-acetylglucosamine; GlcN=glucosamine; UA=uronic acid; S=sulfate; and Gal=galactose.

38. (Original) The method of claim 27, wherein determining the target quantity comprises a mass spectrometric analysis.

39. (Original) The method of claim 27, wherein determining the target quantity comprises a chromatographic assay, an immunoassay, liquid chromatography, anion exchange chromatography; size exclusion chromatography, or combination thereof.

40. (Original) The method of claim 27, wherein the target animal has received a MPS therapy.

41. (Original) The method of claim 40, wherein the MPS therapy comprises a bone marrow transplant ("BMT") or a MPS enzyme replacement therapy.

42. (Original) The method of claim 27, wherein the target biological sample and the reference biological sample contain an internal standard.

43. (Original) The method of claim 27, further comprising treating the target animal with a MPS therapy, wherein the MPS therapy is based on the deviation of the target quantity as compared to the reference quantity.

44. (Original) The method of claim 43, wherein the MPS therapy comprises a bone marrow transplant ("BMT") or a MPS enzyme replacement therapy.

45. (Original) The method of claim 40, wherein the internal standard comprises a deuterated N-acetylglucosamine-6-sulfate ("GlcNAc6S(d3)").

46. (Original) The method of claim 40, wherein the internal standard comprises a non-physiological oligosaccharide that is similar to the oligosaccharide being investigated.

47. (Original) The method of claim 46, wherein the non-physiological oligosaccharide is derived from a chondroitinase digestion of chondroitin sulfate having an unsaturated uronic acid at the non-reducing end.

48. (Original) The method of claim 27, wherein the MPS disease is MPS-I, MPS-II, MPS-IIIA, MPS-IIIB, MPS-VI, MPS-IIIC, MPS-IIID, MPS-IV, or combination thereof.

49. (Original) The method of claim 27, wherein the target animal is newborn baby.

50. (Original) The method of claim 27, wherein the target MPS biomarker is contacted with a an enzyme that characterizes a particular MPS disease subtype, wherein contacting occurs before determining the quantity of the target MPS biomarker.

51. (Original) The method of claim 50, wherein the enzyme comprises α-L-iduronidase.

52. (Original) A kit for diagnosing a pre-clinical status, or a clinical status of a mucopolysaccharidoses ("MPS") disease in a target animal comprising:

(a) an oligosaccharide derivatization agent;

(b) an acid solution;

(c) an internal standard;

(d) a solid phase extraction column;

(e) a solid phase extraction column wash solution; and

(f) an oligosaccharide elution solution.

53. (Original) The kit of claim 52, wherein the oligosaccharide derivatization agent is a solution comprising: 1-phenyl-3methyl-5-pyazolone ("PMP").

54. (Currently Amended) The kit of claim 52, wherein the acid solution is a vial comprising: formic ~~acid~~ acid.

55. (Original) The kit of claim 52, wherein the internal standard comprises: a deuterated N-acetylglucosamine-6-sulfate ("GlcNAc6S(d3)").

56. (Original) The kit of claim 52, wherein the internal standard comprises a non-physiological oligosaccharide that is similar to the oligosaccharide being investigated.

57. (Original) The kit of claim 56, wherein the non-physiological oligosaccharide is derived from a chondroitinase digestion of chondroitin sulfate having an unsaturated uronic acid at the non-reducing end.

58. (Original) The kit of claim 52, wherein the solid phase extraction column comprises a C18 reverse phase column.

59. (Original) The kit of claim 52, wherein the solid phase extraction column wash solution comprises: $CHCl_3$.

60. (Original) The kit of claim 52, wherein the oligosaccharide elution solution comprises: CH_3CN and formic acid.

61. (Original) A method for diagnosing a pre-clinical status, or a clinical status, of a mucopolysaccharidoses ("MPS") disease in a target animal comprising:

(a) determining a target quantity of a target MPS biomarker from a target biological sample taken from the target animal; and

(b) comparing the target quantity to a reference quantity of a reference MPS biomarker;

wherein,

the target MPS biomarker is the same or equivalent to the reference MPS biomarker, and each of the target MPS biomarker and the reference MPS biomarker is an oligosaccharide, and the oligosaccharide is a that comprises: HNAcS; HNAcS2; HNS-UA; UA-HNAcS; HNAcS-UA; UA-HNAc-UA-S; (HNAc-UA)2-S; (HNAc-UA)2(S)2; or hexasac, wherein, UA=uronic acid; HNAc=N-acetylhexosamine; HN=hexosamine; Hex=hexose; (S)=sulfate not having a sugar residue defined;

the target MPS biomarker and the reference MPS biomarker are derivatized with a derivatizing agent prior to determining the quantity of the target MPS biomarker and the

quantity of the reference MPS biomarker, wherein, the derivatizing agent comprises 1-phenyl-3-methyl-5-pyrazolone ("PMP");

the target quantity and the reference quantity are normalized to creatinine; the reference quantity is determined from a reference animal, or group of reference animals, having a known MPS clinical status;

a deviation of the target quantity from the reference quantity is a pre-clinical or clinical indication of the MPS disease, an indication of a progression of the MPS disease, or an indication of a regression of the MPS disease, and the MPS disease is selected from a group comprises: MPS I, MPS II, MPS IIIA, MPS IIIB, MPS IIIC, MPS IIID, MPS IVA, MPS VI, or multiple sulfatase deficiency;

the target quantity and the reference quantity are determined using a mass spectrometry method; and

an internal standard is utilized to accurately determine the target quantity and the reference quantity, wherein the internal standard comprises a deuterated N-acetylglucosamine-6-sulfate ("GlcNAc6S(d3)").